Remarks

Reconsideration of this Application is respectfully requested. Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

I. Status of the Claims

Upon entry of the foregoing amendment, claims 1 through 286 are pending in the application, with 1, 21, 35, 65, 119, 123, 130, 147, 172-175, 186, 196, 216, and 228 being the independent claims. Claims 1-29, 35-64, 69-72, 75-81, 96-185, 187, 191-194, 196-205, and 213-286 have been withdrawn. Claims 30, 31, 65, 186, 188 and 206 are hereby amended. These changes are believed to introduce no new matter, and their entry is respectfully requested.

The present application is believed to be in condition for immediate allowance. Prompt notice to that effect is respectfully requested.

II. The Amendments

The pending claims are directed to methods for modifying the glycosylation profile of a polypeptide produced by mammalian host cells that contain nucleic acid molecules comprising sequences encoding fusion glycosyltransferases, methods for producing and isolating polypeptides in host cells that express at least one nucleic acid encoding a fusion polypeptide having either β(1,4)-N-acetylglucosaminyltransferase III activity or β(1,4)galactosyltransferase activity, and methods for producing and isolating

polypeptides in host cells that express at least one nucleic acid encoding a fusion polypeptide having GnT III activity and at least one nucleic acid encoding a polypeptide having Man II activity.

Claims 30 and 31 have been amended to include the limitations of claim 1. In addition, these claims have been amended to specify that fusion polypeptides are produced in *mammalian* host cells. Thus, as presently amended, claims 30 and 31 include the *mammalian* host cell limitation and the recitation, "an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has β(1,4)-N-acetylglucosaminyltransferase III activity or β(1,4)-galactosyltransferase activity and comprises the Golgi localization domain of a Golgi resident polypeptide."

Claims 65 and 186 have also been amended to indicate that the fusion polypeptides used in the claimed methods are produced in *mammalian* host cells. Support for the amendments may be found, *inter alia*, at paragraph 95 of the present application, and elsewhere throughout the application.

Accordingly, no new matter is believed to have been added by these amendments and their prompt entry is respectfully requested.

III. The Rejections

A. Rejection Under 35 U.S.C. § 102(b)

Claims 30-32, 34, 65-68, 73, 74, 82-95, 186, 188-190, and 206-212 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Russell *et al* (WO 01/29242). Applicants respectfully traverse the rejection. Solely in an effort to expedite prosecution, and without acquiescing to the propriety of the rejection, Applicants have

amended claims 30, 31, 65, and 186 to include the limitation that the methods require producing the fusion glycosyltransferases in *mammalian* host cells. In so far as the rejection may apply to the amended claims, Applicants provide the following comments.

Russell *et al.* teach fusion glycosyltransferases in *plant cells* and require the specific use of early-pathway *plant* Golgi localization domains (the "CMS" regions) to modify the glycosylation profile of polypeptides. *See* pages 69-71 of Russell *et al.* Russell *et al.* do *not* teach fusion polypeptides having β(1,4)-N-acetylglucosaminyltransferase III activity or β(1,4)-galactosyltransferase activity *and comprising the Golgi localization domain of a mammalian Golgi resident polypeptide.*

In fact, Russell *et al.* teach away from such constructs by teaching that plant cells are the desired cells for practicing the technology discussed therein. With respect to host cells (including mammalian host cells) other than the preferred plant cells, Russell *et al.* state:

> *These hosts, however, may suffer from any or all of the following disadvantages*: expensive fermentation, low yields, secretion problems, inappropriate modifications in protein processing, high operating costs, difficulties in scaling up to large volumes, contamination that kills the host culture, and potential contamination by virus or prior pathogens. *For these reasons, existing eukaryotic hosts are unable to provide high-volume, low cost protein production of heterologous proteins.*

(WO 01/29242 at page 2, lines 25-30.) With respect to mammalian host cells specifically, Russell *et al.* state:

> Moreover, *although mammalian cells are capable of correctly folding and glycosylating bioactive proteins, the quality and extent of glycosylation can vary with different culture conditions among the same host cells.*

> . . . To that end, *plants* represent a suitable alternative to other host systems because of the advantageous economics of growing plant crops, plant suspension cells, and tissues such as callus, the ability to synthesize proteins in storage organs like tubers, seeds, fruits and leaves; and the ability of plants to perform many of the post-translational modifications previously described.

(WO 01/29242 at page 2, line 31, through page 3, line 15.)

As Russell *et al.* do not teach, either expressly or inherently, this feature of the claimed invention, Applicants respectfully assert that Russell *et al.* do not anticipate the claimed invention. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

B. Rejections Under 35 U.S.C. § 103

Claim 33 is rejected under 35 U.S.C § 103 as allegedly unpatentable over Russell *et al.* (WO 01/29242) in view of Umaña *et al.* (*Nat. Biotech.*, 1999). The Examiner states that Russell *et al.* teach methods for modifying the glycosylation profile of an IgG, and Umaña *et al.* teach the production of IgG1 antibodies. Applicants respectfully traverse the rejection.

As Applicants have amended claims 30 and 31 to include the limitation that the methods require using fusion glycosyltransferases produced in *mammalian* host cells and claim 33 depends indirectly from both claims 30 and 31, claim 33 incorporates the limitations of claims 30 and 31. In so far as the rejection may apply to the amended claim, Applicants provide the following comments.

As discussed above, Russell *et al* neither teach nor suggest methods of modifying the glycosylation profile of polypeptides in *mammalian* host cells expressing fusion

glycosyltransferases, and thus fail to anticipate or render obvious the methods of the present invention. Umaña *et al.* do not cure the deficiencies of Russell *et al.* Accordingly, Applicants respectfully request that this rejection be withdrawn.

IV. Other Matters

Claims 30-34 have been rejected for depending from a non-elected claim (claim 1). Claims 30 and 31 have been amended to include the limitation of claim 1 which recites "an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has β(1,4)-N-acetylglucosaminyltransferase III activity or β(1,4)-galactosyltransferase activity and comprises the Golgi localization domain of a Golgi resident polypeptide." These changes introduce no new matter, and their entry is respectfully requested. Based on the above amendment, Applicants respectfully request that the Examiner reconsider and withdraw the objection to claims 30-34.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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